REMARKS

The above amendments are presented in response to the Office Action dated November 30, 2006. Claims 1, 2, 4-12, 14-16, 18 and 19 are pending in the application. Claims 1, 2, and 4-12 have been amended. Claims 15, 16, 18 and 19 have been canceled. Support for the terms "composition" and "pharmaceutically acceptable carrier" can be found in the specification at page 1, line 8 and page 26, line 11, respectively. Support for the amendments to claim 11, and 12 can be found in now-canceled claims 15. No new matter has been added.

Amendment of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the invention to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

In light of the claim amendments and the following remarks, Applicant respectfully request that the Examiner withdraw the rejections and pass this case to issuance.

Objections to the Drawings

The Examiner objects to "the resolution and clarity" of Figures 3, 4, 7-10, and 13 on page 3 of the November 30, 2006 Office Action. However, on page 2, the Examiner states that the objection to Figure 7 has been withdrawn. Accordingly, Applicants have not amended Figure 7. In addition, Applicants respectfully request that the Examiner provide details as to why Figure 13, which clearly depicts a bar graph, is objectionable. Applicants believe that the Examiner did not intend to object to all subparts of the Figures contained above.

In response to the objection to the Drawings, Applicants have deleted Figures 3A, 3B, 3C, 4B-K, 8A-8I, and 8K-8M, 9A-L, 10A-I, 11A-I and reference thereto in the Specification, and have submitted replacement drawing sheets renumbering Figures 3D-H as 3A-E, Figure 8J as 8A, Figures 12A-D as 9A-D, and Figure 13 as Figure 10. Applicants have amended the specification deleting Figure numbers of the deleted Figures and renumbering the Figures as

described above. Accordingly, Applicant respectfully requests that the Examiner withdraw the objections to the drawings.

Objections to the Specification

The Office Action states that there is no description of Figs 2E-2H. In response, applicant has amended the brief description of the drawings to correct this deficiency.

The Office Action objects to the labeling of the x-axis of Fig. 12D. In response, applicant has amended the labeling of the x-axis to clarify the graph.

Accordingly, Applicant respectfully requests that the Examiner withdraw these objections.

Rejection of Claims 1, 2, 4-12, 14-16, 18 and 19 Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1, 2, 4-12, 14-16, 18 and 19 under 35 U.S.C. § 112, first paragraph, because the specification "while being enabling for a neurological vaccine comprising an AAV vector encoding NMDAR1 and a method of ameliorating brain damage associated with epilepsy or stroke in a rat, via prior oral administration of said vaccine, does not reasonably provide enablement for a neurological vaccine comprising any vector encoding any NMDA receptor antigen for treatment of any injury or disease, and a method of modulating a neurological disorder in any subject" Applicant respectfully traverses this rejection.

While Applicant disagrees with the rejection, the claims have been amended to expedite prosecution. As amended, independent claim 1 and 12 recite a "composition" comprising a "vector comprising a nucleic acid sequence encoding for an N-methyl-D-aspartate (NMDA) receptor antigen capable of being expressed in a subject", and "a pharmaceutical acceptable carrier."

As amended, the claims are directed to a "composition" comprising a specific antigen, *an N-methyl-D-aspartate (NMDA) receptor antigen*, and "a pharmaceutical acceptable carrier."

Applicant disagrees with the Examiner's statement that "the claims continue to cover treatment of *any* neurological injury or disease." Amended independent claim 1 recites a *composition*, not a treatment. Accordingly, claim 1 does not recite its potential uses. In addition, independent method claim 12 and dependent claim 11, have been amended to recite "method for ameliorating or delaying onset of epilepsy, stroke, or decreased cognition in a subject." The amendments to the claims obviate most of the rejections under 35 U.S.C. § 112, first paragraph. The remaining issues are addressed below.

The Office Action asserts that the claims are not enabled because of the "unpredictability inherent to the art of DNA vaccination". Applicants note that for the claimed method to be enabled, the method does not necessarily have to be able to cure the disorders (e.g., epilepsy, stroke, decreased cognition), so evidence of regression is not necessary for enablement. One of ordinary skill in the art would recognize that the claimed method is useful for the recited disorders, and s/he can "make and use" the claimed invention without any undue experimentation. There is no reason to believe that the method will not help treatment of the disclosed disorders, and *in vivo* or clinical data is not necessary for patentability analysis.

The references cited in the 11/21/05 Office Action recite five factors needed for an "ideal vaccine." The Office Action also points to specific language in a number of references to imply that "true success [with gene therapy] has been limited." (See, Office Action 11/21/05 page 9). There is no requirement that claimed invention be "ideal" or that it achieves "true success." In fact, the claimed invention is enabled even if the claims encompass "inoperative subject matter"::

> [t]he presence of in operative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v E.I. du Pont de Nemours & Co.*, 750 F.2d. 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). MPEP 2164.08(c)

Furthermore, substantial progress has been made in this area of scientific research. In the area of gene therapy, a great number of successes, both *in vitro* and *in vivo*, have been documented with various types of expression vectors. For example, even the cited Verma et al.

(1997 Nature 389: 239-242) reference, relied upon by the 11/21/05 Office Action, states that "adenoviral vectors are extremely useful if expression of the transgene is required for short periods of time". The Shoji *et al.* (2004) reference cited in the 11/21/05 Office Action states that the "data suggests that the pharmacokinetics/pharmacodynamics characteristics of oligonucletides is more favorable *in vivo* than initially thought" and that "[d]espite initial expectation, oligonucleotides after the oral administration was relatively stable and hold the biological activities" (See Shoji *et al.* page 791, first column and p 792, second column).

In addition, the 11/21/05 Office Action points to McCluskie *et al.* as showing that the "*strength* and *nature* of the immune responses to administration of DNA vaccines varies between species." Applicant points out that while the *strength* of the immune response may be varied, an immune response was nonetheless present. Applicant directs the Examiner to the last paragraph on page 296, where McCluskie states that "[w]hile efficacy in murine models has preceded the successful development of many human vaccines, it is probably safe to say that any vaccine that works in a human will work in a mouse." Again, the Examiner is reminded that evidence that the claimed invention produces an "ideal" response is not required.

The Babiuk (1999) reference goes on to say that "expression of the foreign gene in vivo should lead to an immune response to the protein produced by the gene. This was shown to be the case with genes from a wide variety of pathogens including viruses, bacteria and parasites...it appears that even very small amounts of protein are sufficient to induce both cellular and humoral immune responses following plasmid introduction into a wide variety of species." (See, Babiuk, page 1593, first column).

The Office Action asserts on page 7 that the specification has not enabled all possible routes of administration, but that only oral administration is enabled since the guidance provided by the specification "is in the form of general guidance rather than specific guidance." Applicant respectfully disagrees with the Examiner's conclusion of non-enablement. Even if it is scientifically sound to doubt the viability of other, non-exemplified administrative routes, the claimed invention remains enabled, because the claims may encompass "inoperative subject

matter." (See, MPEP 2164.08(b) discussed above). Moreover, contrary to the Examiner's assertion that "contemplation of various routes of administration of a vaccine does not constitute enablement for all modes of administration," the amended claims are enabled in light of the teaching in the specification. The specification gives numerous examples of how to demonstrate that the claimed invention is operative (*See,* for example, Examples2-6).

At page 8 of the Office Action, the Examiner asserts that "the issue is not whether the animal models accurately model the features of the human diseases, but whether the immune response obtained in a rat is predictive of the immune response that would be obtained in other animal species, including humans." Applicant traverses this rejection.

The Examiner has rejected the art recognized models based on the distinction between an animal model accurately modeling human diseases and an animal model accurately modeling human immune responses. While Applicants appreciate the distinction, it appears to be a distinction without a difference. The Examiner is reminded of the standard stated in the MPEP 2164.02, "[a]n *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a disclosed or claimed method invention." An animal model is acceptable where it is recognized in the art that this model correlates to a specific condition. If this has not yet been established in the art, the animal model is acceptable if one skilled in the art would accept the model as *reasonably correlating* to the condition.

The Applicant has demonstrated the claimed invention in animal models accepted by those in the skilled in the art. Specifically, the specification shows that "epilepsy, stroke, or decreased cognition" were decreased following administration of the claimed composition. Thus, the specification has demonstrated the claimed methods in the art recognized animal model.

For all of these foregoing reasons, Applicant respectfully requests that the Examiner withdraw all rejections under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 1, 2, 4-12, 14-16, 18 and 19 Under 35 U.S.C. §112 Second Paragraph

Claims 1, 2, 4-12, 14-16, 18 and 19 have been rejected under 35 U.S.C. § 112, second paragraph as being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Claims 2, 5, 6, 11, 12, 14, 15, 16, 18 and 19 are rejected as being indefinite since they recite the term "neurological disorder." This rejection is moot in light of the claim amendments.

Claims 2, 5, 6, 12, 14, and 15 is rejected based on the term "target protein." Applicant has amended claims 2 and 12 to recite "NMDA receptor." Claims 5, 6, and 14 do not recite the term "target protein," and claim 15 has been canceled.

Claim 12, 14, and 15 have been deemed indefinite based on the claim language. The amendment to independent claim 12, and cancellation of claim 15 obviate this rejection.

Claim 16, 18, and 19 are rejected as indefinite. The cancellation of claims 16, 18, 19 renders this rejection moot.

In light of these amendments, the Examiner is hereby requested to withdraw the indefiniteness rejections.

Rejection of Claims 1, 2, 4-8, 10, 16, 18, 19 Under 35 U.S.C. §102

Claims 1, 2, 4-8, 10, 16, 18, and 19 have been rejected under 35 U.S.C. § 102, as having been anticipated by Lissin *et al.* (PNAS 95: 7097-7102 (1998)). Claims 16-19 have been canceled. Applicant respectfully traverses this rejection.

Lissin et al. simply describes a reagent that can be used in *in vitro* cell cultures to determine localization to synapses. The reagent (NR1) was epitope-tagged at the amino terminus with a signal sequence followed by a hemagglutinin (HA) epitope tag. Accordingly, the vector differs from that of the claimed invention. There is no suggestion or even a reason to assume

that the *HA tagged* NR1 described by Lissin et al. can be expressed *in vivo*, "such that the expressed antigen elicits production of antibodies in a circulatory system of the subject, wherein the antibodies pass across a blood-brain barrier into a central nervous system upon injury."

Furthermore, as amended, the independent claims 1 and 12, recite "a pharmaceutical acceptable carrier." Support for this amendment can be found throughout the specification as originally filed, and specifically at page 26, line 11. Since the Lissin reference merely describes *in vitro* experiments, there is no teaching or motivation to use a pharmaceutical acceptable carrier as required by the independent claims, and claims dependent thereto. Because a claim is anticipated only if each and every element as set forth in the claim is found in a single prior art reference, the Lissin reference does not anticipate the claimed invention. Not only is the claimed invention not anticipated by the Lissin reference, it is also not obvious. There is no suggestion or teaching in the reference that would encourage one skilled in the art to use a reagent for therapeutic uses. Accordingly, the Examiner is respectfully requested to withdraw the novelty rejections.

CONCLUSION

In summary, the above-identified patent application has been amended and reconsideration is respectfully requested for all the reasons set forth above. The Examiner is urged to telephone the undersigned Attorney for Applicant in the event that such communication is deemed to expedite prosecution of this matter.

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Respectfully submitted,

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